



## Complete Summary

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### GUIDELINE TITLE

Deep venous thrombosis.

### BIBLIOGRAPHIC SOURCE(S)

Finnish Medical Society Duodecim. Deep venous thrombosis. In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2004 Mar 2 [Various]. [57 references]

## COMPLETE SUMMARY CONTENT

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INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT

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## SCOPE

### DISEASE/CONDITION(S)

Deep venous thrombosis

### GUIDELINE CATEGORY

Diagnosis

Evaluation

Management

Prevention

Risk Assessment

Treatment

### CLINICAL SPECIALTY

Family Practice

Internal Medicine

### INTENDED USERS

Health Care Providers  
Physicians

## GUIDELINE OBJECTIVE(S)

Evidence-Based Medicine Guidelines collects, summarizes, and updates the core clinical knowledge essential in general practice. The guidelines also describe the scientific evidence underlying the given recommendations.

## TARGET POPULATION

Patients with deep vein thrombosis and those at risk for thromboembolism

## INTERVENTIONS AND PRACTICES CONSIDERED

### Evaluation/Risk Assessment/Diagnosis

1. Risk factor assessment
2. Clinical assessment of signs and symptoms (pain, tenderness, oedema, Homan's sign, swelling, erythema, skin warmth)
3. Doppler ultrasound (compression echography)
4. Venography
5. Measurement of plasma D-dimer by enzyme-linked immunosorbent assay or latex test
6. Scoring the probability of deep venous thrombosis (DVT) using signs and symptoms

### Treatment/Management/Prevention

1. Decide site of treatment (hospital versus home)
2. Mobilization
3. Pharmacotherapy
4. Fibrinolytic therapy (systemic or local), such as tissue plasminogen activator (tPA)
5. Unfractionated heparin
6. Low-molecular-weight heparin (LMWH), such as dalteparin, enoxaparin, nadroparin, tinzaparin
7. Warfarin
8. Thrombectomy
9. Compression bandaging/stockings
10. Vitamin K antagonists
11. Follow-up for complications (e.g., treatment of heparin-induced bleeding complications with deficient blood products [fresh frozen plasma, thrombocytes] or protamine)

## MAJOR OUTCOMES CONSIDERED

- Incidence of complications and cost-effectiveness of treatment (home versus hospital treatment)
- Sensitivity and specificity of diagnostic assessments
- Treatment effect on:

- Incidence of pulmonary embolism
- Incidence of major bleeding
- Frequency of postthrombotic changes
- Recurrence of venous thromboembolism
- Overall mortality
- Adverse effects

## METHODOLOGY

### METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)  
 Hand-searches of Published Literature (Secondary Sources)  
 Searches of Electronic Databases

### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The evidence reviewed was collected from the Cochrane database of systematic reviews and the database of abstracts of reviews of effectiveness (DARE). In addition, the Cochrane Library and medical journals were searched specifically for original publications.

### NUMBER OF SOURCE DOCUMENTS

Not stated

### METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

### RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

- Strong research-based evidence. Several relevant, high-quality scientific studies with homogeneous results.
- Moderate research-based evidence. At least one relevant, high-quality study or multiple adequate studies.
- Limited research-based evidence. At least one adequate scientific study.
- No scientific evidence. Expert panel evaluation of other information.

### METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses  
 Systematic Review

### DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

## METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

## RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

## COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

## METHOD OF GUIDELINE VALIDATION

Peer Review

## DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

The levels of evidence [A-D] supporting the recommendations are defined at the end of the "Major Recommendations" field.

#### Aims

- To prevent pulmonary embolism and post-thrombotic syndrome
- To suspect thrombosis in high risk patients
- Plasma D-dimer test can be used in primary care as the first-line test to rule out deep-vein thrombosis (DVT). If the D-dimer concentration is increased, or DVT is clinically apparent, the patient should be referred for diagnostic imaging investigations.
- A suspected DVT is verified by venography or compression ultrasonography.
- To prevent DVT in immobilised patients: calf muscle exercise, socks that prevent emboli, and, if necessary, prophylactic treatment with subcutaneous low-molecular-weight heparin (LMWH)
- When the diagnosis has been confirmed, DVT can be treated at home or in a general hospital ward. A distal deep calf thrombosis does not cause emboli, and only about 25% of the thrombi reach the femoral level.
- Idiopathic venous thrombosis may be a sign of a malignancy.

#### Risk Factors for Deep Venous Thrombosis

- Immobilisation due to an acute illness, especially if the circulation is simultaneously impaired (e.g. heart failure, paralysis, surgery, infection, long flight)

- Trauma to the lower limbs (fractures in plaster cast in particular)
- Hereditary or acquired coagulation disorder (see EBM guideline on Leg Oedema) (always suspect these aetiologies when no external cause is evident)
- Polycythaemia, essential thrombocytosis
- Use of oral contraceptives, hormone-replacement therapy, especially in smokers
- Previous venous thrombosis
- Pregnancy and the postpartum period (6 weeks), caesarean section, the age of the mother
- Cancer in an active phase
- Central venous catheters, often located in an upper limb.

### Symptoms

- Oedema of the entire leg or calf (for differential diagnosis, see EBM guideline on Leg Oedema)
- Tenderness or ache at rest
- Pain in the calf while walking
- Concurrent pain, tenderness, and oedema are strongly suggestive of DVT (59%). Each sign alone indicates thrombosis in only 11 to 22% of the cases (Wells et al., 1997).
- Often completely asymptomatic, particularly in bed-bound patients in whom the first symptom may be pulmonary embolism. In patients with a hip fracture, the thrombosis often only occurs in the femoral and pelvic areas.
- Almost half of proximal DVTs are associated with either symptomatic or asymptomatic pulmonary embolism.

### Diagnosis

- The probability of a patient having DVT is influenced by his/her predisposition to thrombotic events and whether there is a history of previous venous thrombosis.
- Clinical findings:
  - Oedema of the ankle and lower leg; iliac vein thrombosis oedema of the entire leg
  - Deep calf tenderness on palpation along the involved vein
  - Positive Homans' sign (not always, especially if the patient is in bed rest)
  - Warmth of the skin when compared with the other leg and prominent superficial collateral veins
- Doppler ultrasound examination (see EBM guideline on Doppler Stethoscopy in Diagnostics) to assist diagnosis:
  - Impaired or slowed flow in the popliteal vein when the calf is compressed
  - Slowed flow in the posterior tibial vein when the compression is released
  - In iliac vein thrombosis there is an absence of phasic respiratory signals or a weakened flow sound from the femoral vein when listened to at the groin.
- For differential diagnosis, see the EBM Guideline on Leg Oedema.

## Care Guidelines in Suspected Deep Venous Thrombosis

- The probability of venous thrombosis can be estimated and scored using the below list of signs and conditions (Give 1 point for each finding or condition which is likely to increase the pretest probability of DVT. If a diagnosis other than DVT is highly likely for other reasons, subtract 2 points from the final sum.) (Wells et al., 1997)
  - Cancer that is being actively treated or that has metastasised
  - Paralysis or recent immobilization of a lower limb
  - Bed rest of more than 3 days duration
  - A major operation within 1 month
  - Local tenderness in the calf or in the thigh, around the deep venous trunk. Often indicated as the reason for referral, but when presents alone has poor prognostic value for DVT.
  - More than a 3-cm difference in the circumference of the calves
  - Strong familial predisposition (at least 2 first-degree relatives with a history of venous thrombosis)
  - Even though the studies evaluating the value of risk scoring did not take the use of oral contraceptives and a personal history of a previous DVT into consideration, a point could be allocated for both in clinical adaptations of the scoring system.
- Plasma D-dimer test is used for the exclusion of DVT. (The test is very sensitive, but not as specific. A positive result does not therefore always indicate thrombosis.)
  - If the D-dimer test is negative in a low-risk patient (0 risk points), no further investigations are needed (Kearon et al., 2001). In clinical practice, a negative D-dimer test is also sufficient to exclude DVT in patients who only score one point for palpation tenderness in the calf or thigh.
  - If the first ultrasonographic finding and plasma D-dimer test are both normal in a patient at higher risk, repeated ultrasonography is not necessary.
  - D-dimer concentration may also be increased during normal pregnancy.
- Initial treatment with low-molecular-weight heparin (LMWH) can often be started on the basis of suspicion alone. Any delay in imaging investigations will thus not pose extra risk for the patient.
- Compression ultrasonography is used currently as an early phase investigation. It is sensitive (90%) particularly in proximal thrombosis, less so (50%) in distal thrombosis. Compression ultrasonography is replacing venography, which is useful in the diagnosis of recurrent DVTs.
  - An abnormal ultrasonography finding is an indication for treatment. A normal result in a low-risk patient (0 risk points) excludes venous thrombosis. A normal result with a positive D-dimer in a moderate-risk patient (1–2 risk points) warrants a repeat ultrasonography in 7 days, and in a high-risk patient (3 or more risk points) venography should be performed immediately (Cogo et al., 1998).
  - An abnormal venography (a persistent intravenous filling deficit in at least two projections) is an indication for treatment. A normal result excludes venous thrombosis.

## Treatment

## Basic Rules

- Compression bandaging (see below)
- In proximal thrombosis, early mobilisation is recommended after a few days of heparin therapy.
- Distal, and often also proximal, thrombosis can be treated at a general hospital ward or at home, either by a district nurse or the patient him/herself. Based on individual situations, the treating physician will decide where the treatment should be carried out. Obese patients will need two injections because of the large doses needed. An underweight patient or one with multiple illnesses is not usually suitable for home care. The patient will need written instructions for home care.
- Hospital treatment is indicated if there is
  - severe oedema of the entire leg
  - thrombosis above the groin
  - other coexisting illnesses requiring hospital treatment
- If the treatment is carried out at home, ensure that
  - the injection technique and drug dosage are correct
  - the follow-up of anticoagulation therapy is adequate
  - the patient has instructions regarding compression bandages and stockings
  - the patient is monitored for possible complications (bleeding, emboli)

## Treatment According to the Location and Duration of the Thrombosis

- A high, iliofemoral thrombus or thrombus in the upper extremities with onset within the last 7 days
  - Systemic fibrinolytic therapy, similar to the one given in myocardial infarction, is used in some centres. Its efficacy against post-thrombotic syndrome has not been established (Schweizer et al., 2000). Local fibrinolysis is implemented by introducing a catheter into the thrombus mass. The success of fibrinolysis is monitored by venography. The currently used agent for fibrinolysis is tissue plasminogen activator (tPA). Treatment time is 1–3 days, and the aim is to minimize the time because of the risk of bleeding (Mewissen et al., 1999).
  - The contraindications are the same as for fibrinolytic therapy in myocardial infarction (see EBM guideline on Thrombolytic Therapy and PTCA in Acute ST Elevation Myocardial Infarction [STEMI]). The aim is to decrease the risk of post thrombotic syndrome. The use is limited to young patients with recent, extensive iliofemoral thrombosis or pulmonary emboli with potentially hazardous haemodynamic consequences. Total lysis is rarely achieved because venous thrombi are often old and organised.
  - LMWH (van der Belt et al., 2002; Leizorovicz et al., 1994; DARE-948053, 1999; Leizorovicz, 1996; DARE-970245, 1999; Martineau & Tawil, 1998; DARE-980950, 2000; Hirsh et al., 1995; DARE-963681, 1999; Gould et al., 1999; DARE-999249, 2000) [A] has replaced intravenous (i.v.) heparin. Begin warfarin therapy concomitantly. Heparin may be stopped when International Normalized Ratio (INR) has been within the target range (usually 2.0–3.0) for at least 2 days (Kearon et al., 2001).

- Thrombectomy may be indicated if the viability of the leg is threatened or when the aim is to reduce the severity of post-thrombotic syndrome (Plate et al., 1997).
- Distal thrombosis in a leg or any other thrombosis with onset more than 7 days ago
  - LMWH (e.g., dalteparin 200 IU/kg once daily, enoxaparin 1.5 mg/kg once daily or 1 mg/kg twice daily) (van der Belt et al., 2002; Leizorovicz et al., 1994; DARE-948053, 1999; Leizorovicz, 1996; DARE-970245, 1999; Martineau & Tawil, 1998; DARE-980950, 2000; Hirsh et al., 1995; DARE-963681, 1999; Gould et al., 1999; DARE-999249, 2000) [A]. In patients with increased tendency to thrombosis, the twice daily regimen is recommended. Heparin may be stopped when INR has been within the target range for at least 2 days. The treatment does not necessitate laboratory follow-up. In pregnant women and in patients with renal insufficiency, thrombophilia, or haemophilia, the concentration of active heparin must be monitored. LMWH is at least as effective as ordinary heparin (van der Belt et al., 2002; Leizorovicz et al., 1994; DARE-948053, 1999; Leizorovicz, 1996; DARE-970245, 1999; Martineau & Tawil, 1998; DARE-980950, 2000; Hirsh et al., 1995; DARE-963681, 1999; Gould et al., 1999; DARE-999249, 2000) [A] and causes less thrombocytopenia and paradoxical embolism.
  - Start warfarin therapy concomitantly with heparin (see EBM Guideline on Oral Anticoagulation Therapy for instructions) and continue it according to Table I, below.
  - Bandage the leg from the foot up to the upper thigh. The patient can start to mobilize when the leg has been bandaged.
  - Only about 25% of untreated distal thrombi progress to above the knee. Heparin-warfarin therapy is implemented only if there are no contraindications (Ginsberg, 1996). Distal thrombosis may often occur and receive no anticoagulant treatment; it may remain subclinical or occur while the leg is immobilized within a plaster.
- For the duration of warfarin therapy, see the EBM Guideline on Oral Anticoagulation Therapy.
- Prevention of deep venous thrombosis, see the EBM guideline on the Prevention of Venous Thrombosis.

Table. Duration of anticoagulant therapy is determined individually with the anticipated success of therapy, the patient's other illnesses and age, as well as the risk of recurrence being the decisive factors.

Indication	Duration of Therapy
First episode of thrombosis and a transient or modifiable predisposing factor (surgery, trauma, bed rest, oestrogen therapy)	3–6 months
First episode of thrombosis without a predisposing factor	At least 6 months

Indication	Duration of Therapy
First episode of thrombosis in a patient with cancer, cardiolipin antibodies, combined coagulation disorder, homozygous Factor V Leiden, or prothrombin gene mutation.	12 months to lifetime
Recurring thrombosis without a predisposing factor or in association with increased coagulability of blood	Lifetime

### Treatment of Heparin-induced Bleeding

- If heparin induced severe bleeding occurs, the missing blood products must be replaced (fresh frozen plasma, thrombocytes). Protamine is administered if unfractionated heparin had been used. Protamine is not as effective in counteracting the action of LMWH.
- In 1% of the patients, heparin causes thrombocytopenia (HIT), which is a prothrombotic condition.

### Prognosis

- The risk of recurrence depends primarily on the underlying cause and its possible elimination. The duration of anticoagulation therapy is determined by the severity of the thrombosis and the risk of its recurrence. In idiopathic thrombosis, the risk of recurrence is high, and the treatment time is often long, sometimes even lifelong. Recurrence during well-implemented therapy may suggest malignancy or phospholipid antibody syndrome.
- The condition of the venous valves is the decisive factor when assessing the risk for post-thrombotic syndrome. Anticoagulation therapy prevents the recurrence of the thrombus but does not offer protection for the valves. On the other hand, a recurrence increases the risk of post-thrombotic syndrome manyfold (Prandoni et al., 1996).
- The extent and, particularly, high location (above the groin) of a thrombus have been considered as risk factors for post-thrombotic syndrome, and in these cases fibrinolytic therapy is aimed at protecting the valves. This may be achieved by local fibrinolytic therapy administered by catheterisation (Mewissen et al., 1999). However, this therapy is not readily available and may lead to complications, and each case must be assessed individually.
- An elastic compression stocking reduces the risk of post-thrombotic syndrome and should always be worn (Brandjes et al., 1997) (Kolbach et al., 2004) [A].
  - The leg is bandaged using an elastic bandage starting from the foot, with greater pressure near the ankle and reduced pressure higher up. The bandage is worn for two weeks day and night and is changed at 2–3 day intervals. After this, a compression stocking is fitted. It reduces the risk of post-thrombotic syndrome by approximately 50%. The knee-length stocking is usually used. Compression Class 2 is the most commonly used. The stocking is worn from 6 months to 2 years, sometimes permanently.

## Related Evidence

- Long-term anticoagulant therapy after first episode of venous thromboembolism reduces the risk of recurrence without significantly increasing the incidence of bleeding events (Pinede et al., 2000; DARE-20001014, 2002) [A].
- Treatment of vitamin K antagonists reduces the risk of recurrent venous thromboembolism as long as it is used. However, the absolute risk of recurrence declines over time, while the risk of major bleeding remains (Hutten & Prins, 2002) [A].
- Low-molecular-weight heparins (LMWHs) are equally effective as and safer than vitamin K antagonists in the long-term treatment of symptomatic venous thromboembolism (but they are much more costly and need subcutaneous administration) (van der Heijden et al., 2002) [B].
- The number of adverse events with LMWH during pregnancy is small, but there are no randomized clinical trials (RCTs) comparing LMWH with unfractionated heparin (Ensom & Stephenson, 1999; DARE-991717, 2000) [C].
- The incidence of clinically overt venous thromboembolism in orthopaedic surgery patients with negative venography at discharge and no further pharmacological prophylaxis is less than 2% (Ricotta et al., 1996; DARE-973217, 2000) [B].
- The enzyme-linked immunosorbent assay (ELISA) method is more sensitive than latex test for D-dimer in the diagnosis of venous thromboembolism (deep venous thrombosis or pulmonary embolism) (Becker et al., 1996; DARE-968209, 1999) [C].
- Once daily treatment with LMWH is as effective and safe as twice daily treatment with LMWH for the initial treatment of venous thromboembolism (van Dongen, Mac Gillavry, & Prins, 2003) [A].

## Definitions:

### Levels of Evidence

- A. Strong research-based evidence. Several relevant, high-quality scientific studies with homogeneous results.
- B. Moderate research-based evidence. At least one relevant, high-quality study or multiple adequate studies.
- C. Limited research-based evidence. At least one adequate scientific study.
- D. No scientific evidence. Expert panel evaluation of other information.

### CLINICAL ALGORITHM(S)

None provided

## EVIDENCE SUPPORTING THE RECOMMENDATIONS

### REFERENCES SUPPORTING THE RECOMMENDATIONS

[References open in a new window](#)

## TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Concise summaries of scientific evidence attached to the individual guidelines are the unique feature of the Evidence-Based Medicine Guidelines. The evidence summaries allow the clinician to judge how well-founded the treatment recommendations are. The type of supporting evidence is identified and graded for select recommendations (see the "Major Recommendations" field).

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

- Appropriate diagnosis and treatment of deep venous thrombosis and identification of patient groups at risk
- Prevention of pulmonary embolism and post-thrombotic syndrome in patients at risk
- Prevention of deep venous thrombosis in immobilised patients

### POTENTIAL HARMS

- Streptokinase, tissue plasminogen activator (tPA), heparin, and vitamin K antagonists can cause major bleeding complications.
- Unfractionated and low-molecular-weight heparins can cause thrombocytopenia.
- Local and generalized skin reactions and bleeding complications have been observed in studies in which low-molecular-weight heparin was used for thromboprophylaxis.
- In a systematic review of thromboprophylaxis with low-molecular-weight heparin during pregnancy, the following major maternal events were reported: skin reactions, bleeding complications, thromboembolic events, deep vein thrombosis, bilateral renal vein thrombosis, pulmonary emboli, hepatic infarction, and thrombophlebitis.
- Local thrombolytic therapy administered by catheter can result in complications.

## CONTRAINDICATIONS

### CONTRAINDICATIONS

The contraindications for use of streptokinase in venous thromboembolism are the same as in fibrinolytic therapy for myocardial infarction.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Getting Better  
Staying Healthy

### IOM DOMAIN

Effectiveness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Finnish Medical Society Duodecim. Deep venous thrombosis. In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2004 Mar 2 [Various]. [57 references]

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

2001 Apr 30 (revised 2004 Mar 2)

### GUIDELINE DEVELOPER(S)

Finnish Medical Society Duodecim - Professional Association

### SOURCE(S) OF FUNDING

Finnish Medical Society Duodecim

### GUIDELINE COMMITTEE

Editorial Team of EBM Guidelines

### COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Authors: Editors

### FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

### GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version. Deep venous thrombosis. Helsinki, Finland: Duodecim Medical Publications Ltd; 2003 Sep 4. Various p.

#### GUIDELINE AVAILABILITY

This guideline is included in a CD-ROM titled "EBM Guidelines. Evidence-Based Medicine" available from Duodecim Medical Publications, Ltd, PO Box 713, 00101 Helsinki, Finland; e-mail: [info@ebm-guidelines.com](mailto:info@ebm-guidelines.com); Web site: [www.ebm-guidelines.com](http://www.ebm-guidelines.com).

#### AVAILABILITY OF COMPANION DOCUMENTS

None available

#### PATIENT RESOURCES

None available

#### NGC STATUS

This summary was completed by ECRI on August 28, 2001. The information was verified by the guideline developer as of October 26, 2001. This summary was updated by ECRI on December 9, 2002 and July 1, 2004.

#### COPYRIGHT STATEMENT

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The logo for FIRSTGOV, with the word "FIRST" in blue and "GOV" in red, with a small red star above the "I".

